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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/040,776	01/07/2002	Gary A. Piazza	P-119-CIP-5	3678

7590 01/29/2004

Cell Pathways, Inc.
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EXAMINER	
GITOMER, RALPH J	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/040,776	PIAZZA ET AL.	
	Examiner	Art Unit	
	Ralph Gitomer	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

This application is a continuation of 09/664,035, now abandoned, which is a continuation of 09/046,739, now abandoned, and has identical claims originally submitted in '739, however, the inventive entities are different. An explanation is requested. Please update the related cases in the specification and note that abandoned cases cannot be incorporated by reference because they are not available to the public. And please inform the examiner of any and all related cases, pending, abandoned or allowed. Regarding the priority date of the present application, it is granted only to 3/24/98. Please inform the examiner as to how the specification as originally filed of CIP 08/866,027 differs from 09/046,739 in view of the currently claimed invention.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed. Further, note in the Brief Description of the Drawings, each single drawing should be referred to such as A and B in Fig. 7 and all occurrences.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 25 of U.S. Patent No. 5,858,694. Although the conflicting claims are not identical, they are not patentably distinct from each other because the ratio of cGMP/cAMP is defined in a more detailed manner in the present application.

Claims 1-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of US Patent No. 6,200,771. Although the conflicting claims are not identical, they are not patentably distinct from each other because the ratio of cGMP/cAMP is defined in a more detailed manner in the present application.

Claims 1-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of US Patent No. 6,156,528. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '528 specify adenocarcinoma cells and the claims of the present application do not specify any type of cells.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over US Patent No. 6,156,528, which does not have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being obvious over Piazza et al. (5,858,694)

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application of any unclaimed subject matter prior to the effective U.S. filing date of the reference under 37 CFR 1.131.

Applicant has provided evidence in this file showing that the invention was owned by, or subject to an obligation of assignment to, the same entity as 09/046,739 at the time this invention was made. Accordingly, 09/046,739 is disqualified as prior art

through 35 U.S.C. 102(f) or (g) in any rejection under 35 U.S.C. 103(a) in this application. However, this applied art additionally qualifies as prior art under subsection (e) of 35 U.S.C. 102 and accordingly is not disqualified as prior art under 35 U.S.C. 103(a).

Applicant may overcome the applied art either by a showing under 37 CFR 1.132 that the invention disclosed therein was derived from the invention of this application, and is therefore, not the invention "by another," or by antedating the applied art under 37 CFR 1.131.

Claims 1-4 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over US Patent 6,200,771 which has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Curtis-Prior, Jiang, Blaya, and Earnest.

The present claims are directed to finding compounds to treat neoplasia by finding compounds which are PDE inhibitors defined by increasing cGMP and possibly decreasing cAMP in cells. Methods of determining PDE inhibitors are known in this art, see page 11 of the present specification, and are not distinguished by the present claims as written. And the reverse, changes in concentrations of cAMP and cGMP are known to be caused by PDE inhibitors and no other mechanism or method is disclosed except by PDE inhibition.

Curtis-Prior (Lancet) entitled "Cyclic Nucleotide Phosphodiesterase Activity of Human Normal and Carcinomatous Lung Tissue" teaches on page 1224, it is suggested that chemotherapy designed to block the PDE activity, and thus promote accretion of cAMP and cGMP may provide a means of normalizing cancerous tissue. cAMP concentration appears to be correlated with cell proliferation. On page 1225 column 2 the search for inhibitors of PDE is discussed.

Jiang (Proc Natl Acad Sci USA) entitled "Inhibition of Calmodulin Dependent Phosphodiesterase Induces Apoptosis in Human Leukemic Cells" teaches on page 11236 column 1 second paragraph, selective elevations of cAMP levels in transformed lymphocytes could provide a means to selectively induce apoptosis in these cells. One means of elevating cAMP levels in cells is through the inhibition of PDE activity. PDE-5 is cGMP specific. Throughout the article apoptosis and PDE inhibition is discussed.

Blaya (European J of Pharmacology) entitled "Effect of the Protein Kinase Inhibitors...on Lewis Lung Carcinoma Tumor Progression" teaches on page 99 column 2 first paragraph, three compounds were tested on their anti-tumor activity upon a specific known type of cultured lung carcinoma. One of the compounds, IND, is a well known COX inhibitor. H-7 is a known cAMP dependent protein kinase inhibitor and H-8 is a known cGMP dependent protein kinase inhibitor. The COX inhibitor, IND, was less effective than the control. The highest tumor specific cytotoxicity response was from H-8, a PDE inhibitor.

Earnest (J of Cellular Biochem) entitled "Piroxicam and Other Cyclooxygenase Inhibitors: Potential for Cancer Chemoprevention" teaches on page 156, second paragraph, In addition to COX, NSAID's can inhibit activity of other enzymes including PDE and cGMP-AMP protein kinases which may be central to cancer initiation and promotion. Piroxicam decreases PGE2 production.

The claims differ from the above cited references in that they specify finding new drugs whereas the references test drugs known for enzyme inhibition and other functions for inhibiting neoplasia.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to identify compounds with potential for treating neoplasia by determining their PDE inhibitory activity of the compounds in view of the above references which teach compounds which are known to have inhibitory activity for PDE are also found to be effective for treating neoplasia. It is well known in this art for there to be a known drug which is known to be effective for a given function for many years, such as aspirin for example. Much later the mechanism of action of the drug is discovered which permits other substances to be screened for related desired activity. Additionally, it is also well known for a disease to be treated for years, such as colon cancer prevention, by a number of drugs. Many years later the mechanism of action of the treatment is discovered which permits other substances to be screened for related activity. The cited references teach the mechanism of action of drugs known to be effective for treating neoplasia which are the same as presently claimed. The presently claimed methods of determining activity are conventional and the cutoffs, such as specified in claims 2-4, are readily selected when viewing activity curves of known inhibitors and no unexpected results of the presently claimed cutoffs are seen.

Regarding the methods for determining the PDE activity inhibition, all the presently claimed method steps are well known in this art. It is especially noted which of the known isotypes of PDE intended to be inhibited are not specified in the claims.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The present claims are directed to identifying compounds for treating neoplasia by determining if they increase cGMP and either don't affect or decrease cAMP in cells. Various limits are specified in the claims.

The specification as originally filed does not support the claims. Applicants are requested to specifically point out where in the specification the claimed concentration limits are found. On page 11 of the specification, how to measure cGMP and cAMP by known methods is properly disclosed. However, how such a compound with the desired inhibitory action would then be useful for treating neoplasia is not found. And no compounds which fulfill the requirements of the claims are described. It is not seen that the present assay selects compounds in any fashion for treating any neoplasia.

Further, a reading of the specification would indicate far more than the claimed assay steps would be required to select effective compounds for treating neoplasia.

Claims 1-4 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 line 3 and all occurrences, "the compound to be evaluated" lacks antecedent basis. In claim 1 line 3, "treating" is not understood in context. Claim 1 is indefinite in that the cGMP and cAMP is only determined after contacting the test compound so one would not know if there were any change in concentration. Claim 4 fails to further limit claim 3 from which it depends.

The title of the invention is not aptly descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The abstract does not appear to be directed to the presently claimed invention.

The disclosure is objected to because of the following informalities: The Brief Description of the Drawings appears incomplete, for example, Figs. 7A and B are not specified. On page 3 applications are mentioned but are not available to the public until issued. On page 11 line 3, "gene families" is queried. Appropriate correction is required.

The following prior art pertinent to applicant's disclosure is made of record and not relied upon:

Pamukcu (6,235,776 and 6,235,782) teaches treating neoplasia.

Lee (6,187,756) teaches treating with cAMP effects.

Kaneko (5,760,042) teaches inhibiting phosphodiesterases.

Tanaka (5,728,563) teaches a novel phosphodiesterase.

Satoh (4,115,538) teaches an assay for cAMP and cGMP.

Leskovar (6,156,312) teaches reducing cAMP:cGMP ratio in cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Ralph Gitomer
Primary Examiner
Art Unit 1651

RALPH GITOMER
PRIMARY EXAMINER
GROUP 1200

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